CHAPTER 2

REVIEW OF LITERATURE

As Paul A.M. Dirac once said "the measure of greatness in a scientific idea is the extent to which it stimulates thought and opens up new lines of research'' present chapter also intends to measure the greatness and to open up new lines of present and imminent aspects of our investigation entitled ***"Morbidity Status and Gut Health of Normal and Undernourished School Going Children and It's Alteration Upon Feeding Them With Fructooligosaccharide Incorporated Ice-Cream".***

Following flow will be followed to read the collected literature about the present research

2.1. Undernutrition

2.2. Global scenario of Undernutrition

2.3. National scenario of Undernutrition

2.4. Regional scenario of Undernutrition

2.5. Undernutrition in school going children

2.6. Factors affecting nutritional status of children

2.7. The vicious cycle of Undernutrition and Infection

2.8. Role of Immunity and Immunoglobulin A (IgA) in nutrition and infection

2.9. Preventional strategies for Undernutrition

2.10. The intestinal microbiota

2.11. Metabolomics of colonic microbiota in the gut

2.12. Gastrointestinal health and its significance in immunity and Undernutrition

2.13. Factors affecting intestinal microbiota and health

2.14. Role of Prebiotics in enhancing good gutmicroflora viz. Bifidobacteria and Lactic acid bacteria

2.15. Evolution of Fructooligosaccharide (FOS) as a prebiotic

2.16. Role of Fructooligosaccharide in enhancing good gut bacteria viz. Bifidobacteria and Lactic acid bacteria and reducing the enteric pathogens (E.coli)

2.17. Role of FOS in improving immunity and reducing morbidity especially diarrhea, common colds; constipation; flatulence and gut health

2.18. Role of FOS in improving the nutritional status of children

2.1 Undernutrition

Nutrition is a core pillar of human rights and development. Undernutrition (often called as Malnutrition) jeopardizes children's survival, growth, and development, and it slows national progress towards achieving development goals. Undernutrition is often an invisible and silent emergency.

Children of today are citizens of tomorrow, which is why it is extremely important to ensure proper health care facilities as well as adequate nutritional intake for the children. It is now globally acknowledged that investment in human resource development is a pre requisite for any nation.

India is a home to more than one billion people, of which 42 per cent are children. Nineteen per cent of world's children live in India. Since 1947, India has made substantial progress in human development. Still the manifestations of malnutrition are at unacceptable levels [Mehrotra *et al.,* 2011].

Under-nutrition is the outcome of insufficient food intake and repeated infectious diseases. it includes being underweight for one's age, too short for one's age (stunted), dangerously thin for one's height (wasted) and deficient in vitamins and minerals (micronutrient malnutrition) [UNICEF, 2006].

In his article entitled Malnutrition and Undernutrition, Shetty (2003) elaborated that "the terms '**malnutrition'** and '**undernutrition**' are often used loosely and interchangeably. Malnutrition refers to all deviations from adequate and optimal nutritional status, including energy undernutrition and over-nutrition (obesity is a form of malnutrition). The term 'undernutrition' is used to refer to generally poor nutritional status, but also implies underfeeding". He further explains "**Malnutrition** arises from deficiencies of specific nutrients or from diets based on inappropriate combinations or proportions of foods; for example, goitre, scurvy, anaemia and xerophthalmia are forms of malnutrition caused by inadequate iodine, vitamin C, iron and vitamin A, respectively. Malnutrition can also result from excess nutrient losses or utilization. **Undernutrition** is caused primarily by an inadequate intake of dietary energy, regardless of whether any other specific nutrient is a limiting factor".

Nagati *et al.* (2003) similarly mentioned that Under-nutrition is a condition caused by a lack of food of good nutritional value combined with interaction from infections. Micronutrient deficiency is caused by poverty, food insecurity, lack of knowledge, and lack of distribution of adequate resources.

Undernutrition impedes motor, sensory, cognitive and social development, and therefore undernourished children will be less likely to benefit from schooling, and will consequently have lower income as adults [Arunkumar and Hidhayathulla, 2015].

Srivastava *et al.* (2012) also said "Undernutrition in childhood was and is one of the reasons behind the high child mortality rates observed in developing countries. Chronic undernutrition in childhood is linked to slower cognitive development and serious health impairments later in life that reduce the quality of life of individuals".

The consequences of child undernutrition for morbidity and mortality are enormous – and there is, in addition, an appreciable impact of undernutrition on productivity so that a failure to invest in combating nutrition reduces potential economic growth. In India, with one of the highest percentages of undernourished children in the world, the situation is dire [World Bank, 2015].

Although, the latest FAO estimates indicate that global hunger reduction continues: about 795 million people are estimated to be chronically undernourished in 2012–14down more than 100 million over the last decade, and 209 million lower than in 1990–92. In the same period, the prevalence of undernourishment has fallen from 18.7 to 11.3 percent globally and from 23.4 to 13.5 percent for developing countries. It is claimed that 32% of the global disease burden could be removed by eliminating malnutrition [Katona and Apte, 2008].

2.2 *Global scenario of Undernutrition*

Undernutrition affects over 2 billion people. Globally, it is estimated that around 25% of all children in Low and Middle Income Countries (LMICs) (equating to 165 million children) are permanently stunted in their physical growth and cognitive development, compared to 40% in 1990. Global wasting prevalence has reduced in this time from 9% to 8% and underweight rates from 25% to around 16% of all children [Nisbett *et al.*, 2014].

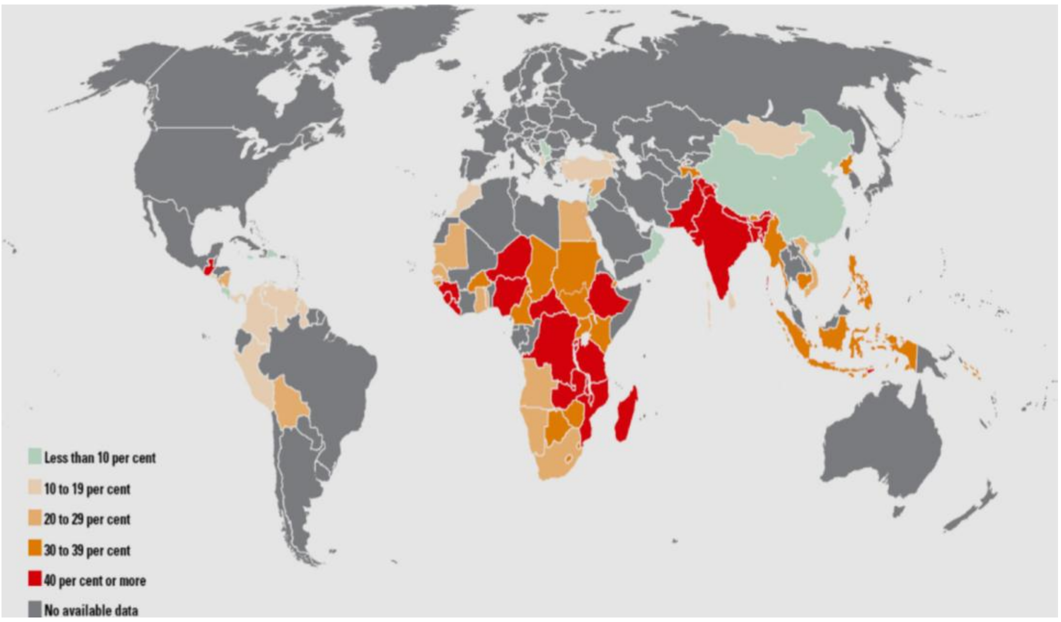

Figure 2.1 Global stunting prevalence – percentage of children under age 5 who are moderately or severely stunted [Source: Nisbett *et al.*, 2014].

Although this positive reduction does contain a hidden disturbing picture of regional disparity and concentration: Stunting rates in East Africa are 42%, 35% in South-Central Asia, and it is currently estimated that 90% of all stunted children reside in just 34 countries (Fig. 2.1). Crucially, these declines are far off targets to end malnutrition in the current generation – it has been estimated that current rates will only bring us half way to meet the World

Health Assembly's newly agreed target committing governments to reduce stunting by 40% (from 2010 levels) by 2025 [Black *et al.*, 2013].

Further, fig 2.2 clearly explains the amateurish status of India among countries with Demographic and Health Survey (DHS). Our neighbors might not be very competent in other economic parameters but they are doing way better in their country's health statistics than us.

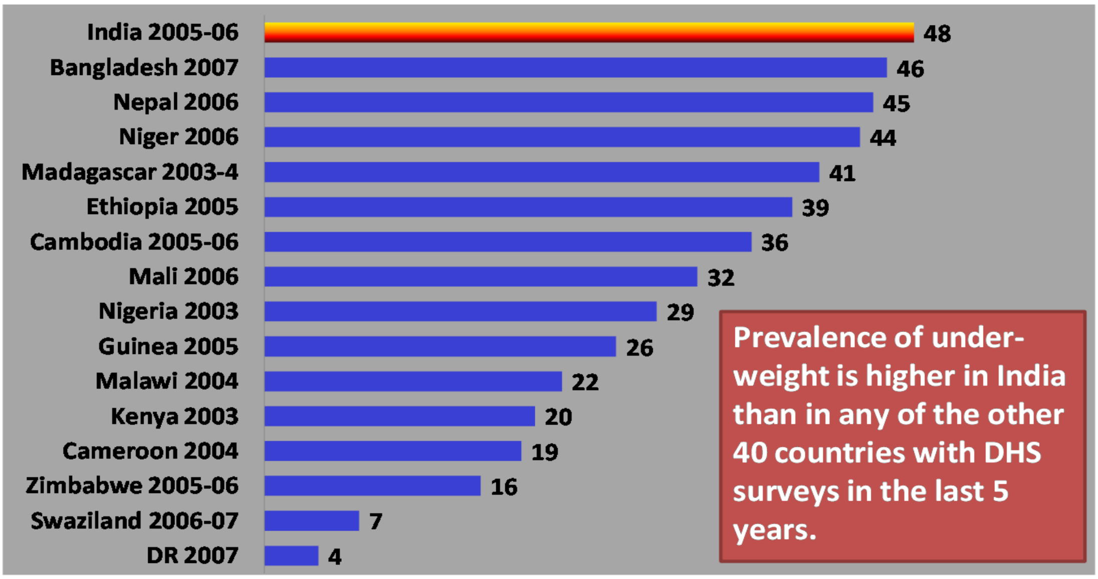

Fig. 2.2Undernutrition (children under five years of age) in India among DHS countries

Singh (2014) in his famous report "Towards a Food Secure India and South Asia: Making Hunger History" revealed "South Asia, comprised of Bangladesh, Bhutan, India, Maldives, Nepal, Pakistan, and Sri Lanka, the region accounts for 23 per cent of the world's population, but generates hardly 2 per cent of the global income. Housing 40 per cent of the world's poor (living on less than US$ 1 a day) and 35 per cent of the world's under-nourished, the region has the highest concentration of poverty and hunger in the world. More than 56 per cent of the world's low-birth-weight babies are born in South Asia. Although the percentage of under nourished people in the South Asian region as a whole during the triennium ending 2003 had declined to 22 per cent from 26 per cent during the base line triennium 1990-92, the number of hungry had increased by over 8 million people during the same period".

In the nutrition literature South Asia is synonymous with unusually high rates of child undernutrition relative to its income levels, as well as sluggish reduction in undernutrition, particularly in **India** [Deaton and Dreze, 2008]. Strikingly, Bangladesh now has lower stunting rates (41.3%) than India recorded in its 2005–06 national nutrition survey (47.5%) or Pakistan did in its 2012 survey (44.8%), despite both countries having higher mean incomes [Headey *et al.*, 2015]. Another study conducted in Nepal enrolled 786 students, of which, 26% of the students were found to be undernourished and 13% stunted, 12% wasted and only 1% both stunted and wasted [Joshi *et al.*, 2011], showing that India is way behind than its closest neighbor in terms of undernutrition stats.

Caulfield *et al.* (2004) indicates that undernutrition in young children contributes significantly toward the global burden of disease. Indeed, childhood underweight is the leading cause of global burden of disease. Deaths attributable to undernutrition encompass 53% of all childhood deaths, echoing the previous estimate of 55% of all deaths to young children.

2.3 *National scenario of Undernutrition*

It is well evident that India is among the worst performers, not only in terms of having highest stats of undernourished children also in dealing with this muddle. The reason of it being ranked at number 5thposition amongst countries with the weakest commitment to ending child malnutrition [Addis *et al.,* 2012], the complete list is shown in fig 2.3.

1. Angola*	**6. Myanmar***
2. Cameroon	**7. Philippines***
3. Democratic Republic of Congo*	**8. Sudan***
4. Cote d'Ivoire	**9. Yemen**
5. India*	
***Indicates countries where World Vision is working to fight poverty**	

Fig. 2.3 Rank of countries based on their commitment to end undernutrition

Public Health Foundation of India (PHFI) and Centre for Disease Control (CDC) are compelled to undertake a purposive short term course entitled "Transforming Nutrition in India: Ideas, Policies and Outcomes" in December 2015 at New Delhi stating "India ranks among the highest in terms of undernourished children".

Popular media houses both print and electronic kept raising this issue time and again (Fig 2.4), but no sigh of relief is yet ascertained in terms of policy changes or deliverables particularly for undernutrition in children.

Fig 2.4 Media coverage of Undernutrition (Malnutrition) in the recent past

Nandi Foundation in their famous HUNGaMA survey report (2011) stated "with 43 per cent of children underweight (with a weight deficit for their age) rates of child underweight in India are twice higher than the average figure in sub-Saharan Africa (22 per cent). The consequences of this nutrition crisis are enormous; in addition to being the attributable cause of one third to one half of child deaths, malnutrition causes stunted physical growth and cognitive development that last a lifetime; the economic losses associated with malnutrition are estimated at 3 per cent of India's GDP annually".

As stated in NFHS III (2005-2006) report (Fig 2.5) the overall prevalence of undernutrition in India was none less than 43% where in stunting and underweight were 20 times as high as would be expected in a healthy, well-nourished population.

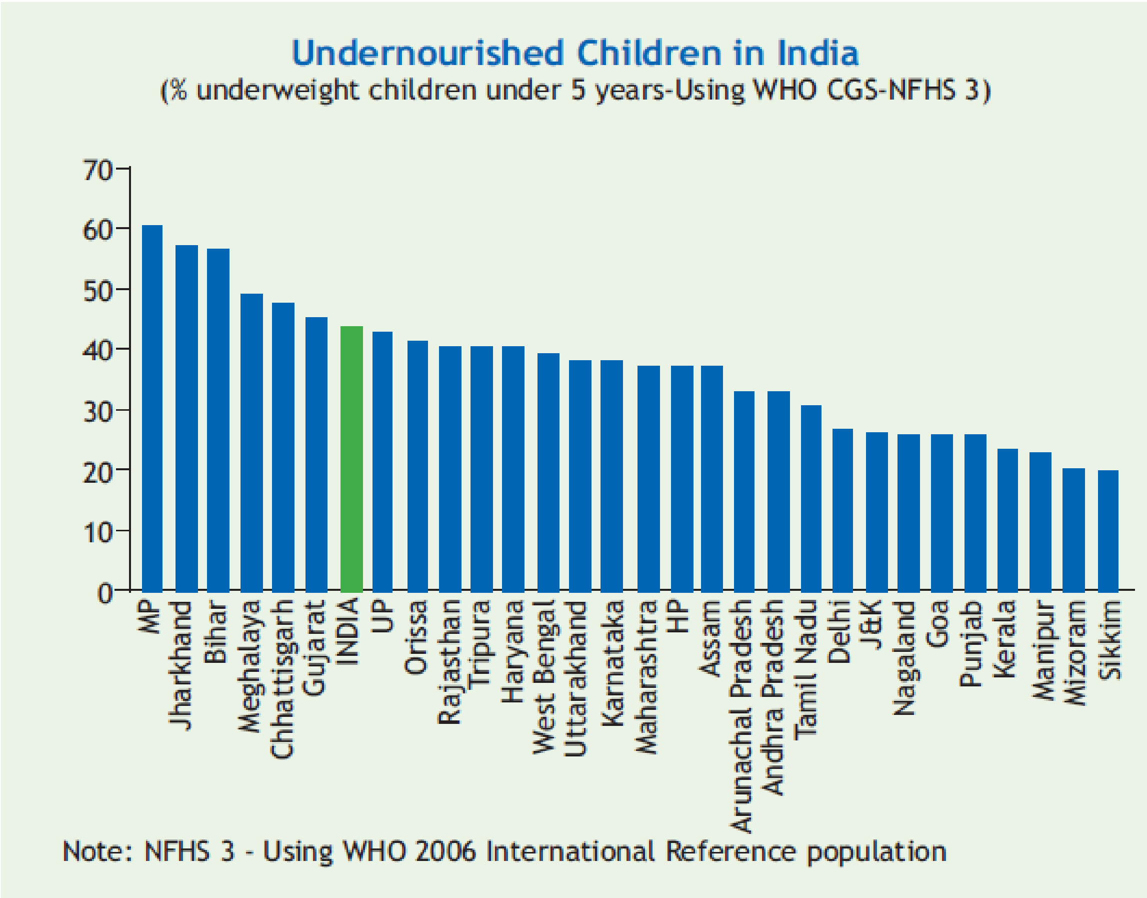

Fig.2.5 State-wise Malnutrition Status

NFHS III depicts that in Maharashtra, Bihar, Madhya Pradesh, Uttar Pradesh, Orissa and Rajasthan, more than one in two children are underweight. Thus, while undernutrition is a national problem, the problem is clearly more acute among certain groups, and inequalities in malnutrition appear to be increasing.

Nair (2007) analyzed the inter-state differentials in malnourishment among children in India on the basis of the National Family Health Survey, 1992-93, 1998-99 and 2005-06 and provided the following table (2.1). In his report he stated that "the prevalence of widespread disparities and these differentials are increasing over time. Also, such differentials do not always vary with the extent of poverty prevalent among the people of the state".

The Economic Times on 4th July 2015 reported "the proportion of hungry children in Gujarat fell to 33.5% from 44.6%, but that remained worse than the national average. The state also showed results worse than average for stunting (42%) and severe stunting (18.5%). States such as Maharashtra with improved access to nutrition and drinking water have done better than other states in improving health of children. According to it, while Madhya Pradesh cut the proportion of its children who go hungry to 36% from 60%, Bihar reduced it to 37% from 56%".

Table 2.1Child Malnourishment in Indian States, 1998-99 and 2005-06

State	Malnourished Children (Per Cent)	
	1998-99	2005-06
Sikkim	20.6	22.6
Nagaland	24.1	29.7
Arunachal Pradesh	24.3	36.9
Kerala	26.9	28.8
Manipur	27.5	23.8
Mizoram	27.7	21.6
Goa	28.6	29.3
Punjab	28.7	27
Jammu and Kashmir	34.5	29.4
Haryana	34.6	41.9
Delhi	34.7	33.1
Assam	36	40.4
Tamil Nadu	36.7	33.2
Andhra Pradesh	37.7	36.5
Meghalaya	37.9	46.3
Uattarakhand	41.8	38
Tripura	42.6	39
Himachal Pradesh	43.6	36.2
Karnataka	43.9	41.1
Gujarat	45.1	47.4
West Bengal	48.7	43.5
Maharashtra	49.6	39.7
Rajasthan	50.6	44
Uttar Pradesh	51.8	47.3
Madhya Pradesh	53.5	60.3
Bihar	54.3	58.4
Jharkhand	54.3	59.2
Orissa	54.4	44
Chhattisgarh	60.8	52.1
India	47	45.9

Note: The states are arranged in ascending order of per cent malnourishment among children in 1998-99.**Source: Nair (2007)**

Above figures made Smith (2015) express her worries in her publication entitled "The great Indian calorie debate: Explaining rising undernourishment during India's rapid economic growth" she stated "despite India's remarkable economic growth over the last decade, many children still struggle to meet their most basic needs, including access to sufficient food and health care. The prevalence of undernourishment in India – the percent of people consuming insufficient calories to meet their energy requirements – has been rising steadily since the mid-1980s. Paradoxically, this period has been one of robust poverty reduction and rapid economic growth. The reasons for the apparent reductions in calorie consumption underlying increased undernourishment have been the subject of intense debate both within India and internationally”.

2.4 *Regional scenario of Undernutrition (Gujarat)*

With a population of 60 million, representing five per cent of India's population, Gujarat's economic development has often been acclaimed as being a highly effective growth and private sector-driven model. In fact, the average growth rate of GDP in Gujarat over the past two decades has been higher than the national average, and more balanced than the other high growth-rate states. However, in terms of overall social development, Gujarat has many more miles to cover to ensure that its economic growth translates into improved and sustainable human development. In the sphere of social development, one of the main challenges faced by Gujarat is the high prevalence of **child under-nutrition**, coupled with a slow reduction in the Infant Mortality Rate (IMR) and Maternal Mortality Ratio (MMR) [UNICEF, Gujarat, 2015].

Women and Child Development Minister of Gujarat, in a written reply to the State Assembly (Gujarat) revealed that, there are at least 6.13 lakh children in 14 districts who are malnourished or extremely malnourished as of August 2013. The district of Ahmedabad, considered to be the commercial capital of the State, had the highest – 85,000-plus – children who are malnourished or severely malnourished. She further added that there are 54,975 malnourished children and 3,860 extremely malnourished children in Ahmedabad city" alone. [The Hindu, October 5, 2013].

As reported by a daily e-paper DNA [DNA India, 27 February 2014] "the number of malnourished and highly malnourished children is more than

55,000 in Banaskantha, nearly 33,800 in Surendranagar and around 7,500 each in Junagadh and Gir Somnath. There are over 5,500 highly malnourished children in Surat, over 3,500 in Surendranagar, more than 2,800 in Banaskantha, around 2,400 in Anand, 2,270 in Kheda and 2,200 in Panchmahals. Among other districts, there are over 1,000 highly malnourished children in Amreli, Sabarkantha and Aravalli. The number ranges from 566 to 893 for smaller districts like Mahisagar, Gir Somnath and Navsari" of Gujarat state.

Government of Gujarat is reported to be spending a whooping amount of almost Rs. 500 crore every year to curb malnutrition. But, the figures show that the desired result is still a far cry [DNA India, 27 February 2014].

After a span of 9-10 months some good news arrived in Gujarat, as the number of moderately and severely malnourished children in the state has reduced from 13.30 lakh in 2011-12, to 9.07 lakh in 2013-14. Even the children admitted to the Nutrition Rehabilitation Centers (NRCs) in Gujarat have gone down. The number of children in these NRCs (set up to address the severe under-nutrition and underlying complications) have gone down to 9200 in 2013-14 from 17,500 in 2012-13. Strangely, the number of NRCs increased to 120 in 2013-14 from 109 a year ago. [Indian Express, 19th December 2014].

Table 2.2. Departmental work on Undernutrition (2007-2010)

Researcher	Place	Age (years)	Prevalence
Kuruvilla and Shah, 2007	Urban slums of Vadodara	10-19	Underweight 32.7%, Stunting 70.7%, Thinness 48.5%
Sharma and	Vadodara	Adolescent	Underweight 68.2%

Dave 2009	(rural)		Stunting 42.8% Thinness 48.2%	
Nambiar and Roy 2010	Chotta udepur taluka	Adolescent School Children	Thinness 44.7% Stunting 29.2%	
Kuruvilla and Mulchandani 2010	Jhagadia Taluka	10-19	Stunting 42.6 % Underweight 63.4 %	
Iyer and Dhaundiyal 2010	Gandhinagar	5-11	Underweight 65.5-71.8% Stunting 35.1-59.5% Thinness 60.2-67.5%	
Iyer and Jain 2011	Vadodara Rural	5-18	Underweight 78.9% Stunting 47% Thinness 65.4%	
Bhoite and Iyer, 2011	Vadodara Rural		Underweight 64% Stunting 31% Thinness 60%	
Dhruv and Karbhari, 2012	Urban Vadodara	8-14	Underweight 58% Stunting 46% Thinness 42%	
Iyer, Gandhi and Mistry, Patel 2013	Vadodara Rural	5-18	Girls Underweight-90%, Stunting - 70% Thinness - 71%.	Boys Underweight-87%, Stunting - 71% Thinness - 74%
Sengar and Sharma 2013	Urban Vadodara	10-19	Underweight – 5.7% Stunting – 14% Thinness-33%	
Dhruv and Tripathi 2014	Rural blocks of Vadodara	6- 13 yrs Girls	Severe Underweight=24%, Severe Stunting=7% Severe Thinness=20% Moderate Underweight- 37%, Moderate Stunting- 24% Moderate Thinness- 27%	
Gandhi, Desai 2014	Rural blocks of Vadodara	6- 13 years Boys	Severe Underweight=27.9%, Severe Stunting=7% Severe Thinness=24% Moderate Underweight- 35%, Moderate Stunting- 23% Moderate Thinness- 29%	

Studies (Table 2.2) conducted in the Department of Foods and Nutrition, Faculty of Family and Community Sciences, The Maharaja Saiyajirao University of Baroda, Vadodara, during last 7 years revealed the prevalence of undernutrition upto 90% [Gandhi *et al.,* 2013].

In March 2015 Gujarat government claimed that the numbers of malnourished children have decreased over the years. In the changed statistics, **Vadodara** (location of the present study) topped among the cities having maximum number of undernourished children. According to the Ministry of Women and Child Welfare (Gujarat) there more than 6.5 lakh children suffer from malnutrition across the state with **Vadodara** district having the highest number of such malnourished children (65,047), followed by Surat (54,595), Panchmahals (46,594), Ahmedabad (46,360) and Banaskantha (44,995) [DNA, 9th March 2015].

2.5 *Undernutrition in school going children*

Although the World Bank has included school health as one component of its essential public health package for cost effective health program, the nutrition and health of school- age children in the developing world has received a little attention [Singh *et al.*, 2014].

Primary school age is a dynamic period of physical growth as well as of mental development of the child. Research indicates that health problems due to miserable nutritional status in primary school-age children are among the most common causes of low school enrolment, high absenteeism, early dropout, and unsatisfactory classroom performance [Srivastava *et al.*, 2012].

Children belong to 5-12 years age group are vulnerable because of their rapid growth rate. They need more attention and care for the physical and mental development. Physical growth, development and well-being are directly related to the nutritional status [Manna *et al.*, 2011].

One of the major health problems in many developing countries including India is widespread prevalence of undernutrition among primary school children [Bose *et al.*, 2006].

Nutritional deprivation is rampant in children of school age particularly primary school children ranging in magnitude from 20-80%[Fazili *et al.*, 2012]. Since deficient physical growth is naturally reflected in their suboptimal mental achievement [Gonzalez *et al.*, 2007], the assessment of nutritional status of this segment of population is essential for making progress towards improving overall health of the school age children [Fazili *et al.*, 2012].

A North Bengal cross-sectional survey reported that the percentage of mild malnutrition was over 40% in age group 5+ to 8+. The age group of 9+, 11+ and 12+ showed maximum number of moderate malnutrition, 80.01% boys and 77.86% girls were suffering from different degrees of malnutrition [Manna *et al.,* 2011]. Contrarily in the municipal schools of North Kolkata only 31.1% of Under-nutrition was observed by Das *et al*., (2013).

Study conducted in Mumbai by Madan *et al.,* (2014) indicates a high prevalence of underweight in government and private school children (82.7% and 55% respectively) based on BMI percentiles. A high percentage of government school and private school children (69.1% and 39.4%, respectively) were also classified in the category of very less body fat.

In another set of cross-sectional study, conducted by Alim *et al*., (2012) six government primary schools of urban areas of Aligarh city, Uttar Pradesh revealed poor nutritional status of school children receiving mid-day meal every day with the prevalence of stunting in boys and girls as 75.35% and 74.68% respectively and wasting was observed as 86.95% for boys and 76.53% for girls.

Whereas, in Bareilly district of Uttar Pradesh, the prevalence of under-nutrition in both male and female was 44.56% and 37.32% respectively. The prevalence of chronic malnutrition (stunting) in male was 26.31% and in females was 21.37%. The prevalence of acute malnutrition in both males and females according to the BMI-for-age was 38.24% and 34.05% respectively [Singh *et al*., 2014]. In Kamrup district of Assam, one of the study reported

31.25% of undernutrition in the primary school children [Talukdar and Baruah, 2015].

Bhoite and Iyer (2011) in their study conducted in rural school of Vadodara district revealed that malnutrition was highly prevalent with 70% of children being underweight. Stunting was evident in 32.4% of girls and 30.8% boys. The prevalence of severe underweight children was 37% by CDC standards while it was 27% by WHO 2007 standard.

2.6 *Factors affecting nutritional status of children*

As per Government of India's report entitled "Children in India" (2012) "malnutrition is not the result of a single cause; the problem is multifaceted, the causes acting singly or in combination with other complex factors like poverty, purchasing power, health care, ignorance on nutrition and health education, female illiteracy, social convention etc.".

Rodriguez *et al.* (2011) explains that "nutritional status affects every aspect of a child's health, including normal growth and development, physical activity, and response to serious illness. Malnutrition may originate from the deficiency or absence of any nutrient. The establishment and severity of malnutrition depends on the cause, intensity and duration of the nutritional deficiency. It can be caused, primarily, by an inadequate diet or, secondarily, by deficiency in gastrointestinal absorption and/or increase in demand, or even, by an excessive excretion of nutrients".

The best global indicator of children's well being is growth. Poor growth is attributable to a range of factors closely linked to overall standards of living and the ability of populations to meet their basic needs, such as access to food, housing and health care [Joshi *et al*., 2011].

The global dilemma of malnutrition can be understood and addressed with the aid of the framework, shown in Figure 2.6, developed by the United Nations Children"s Fund (2004).

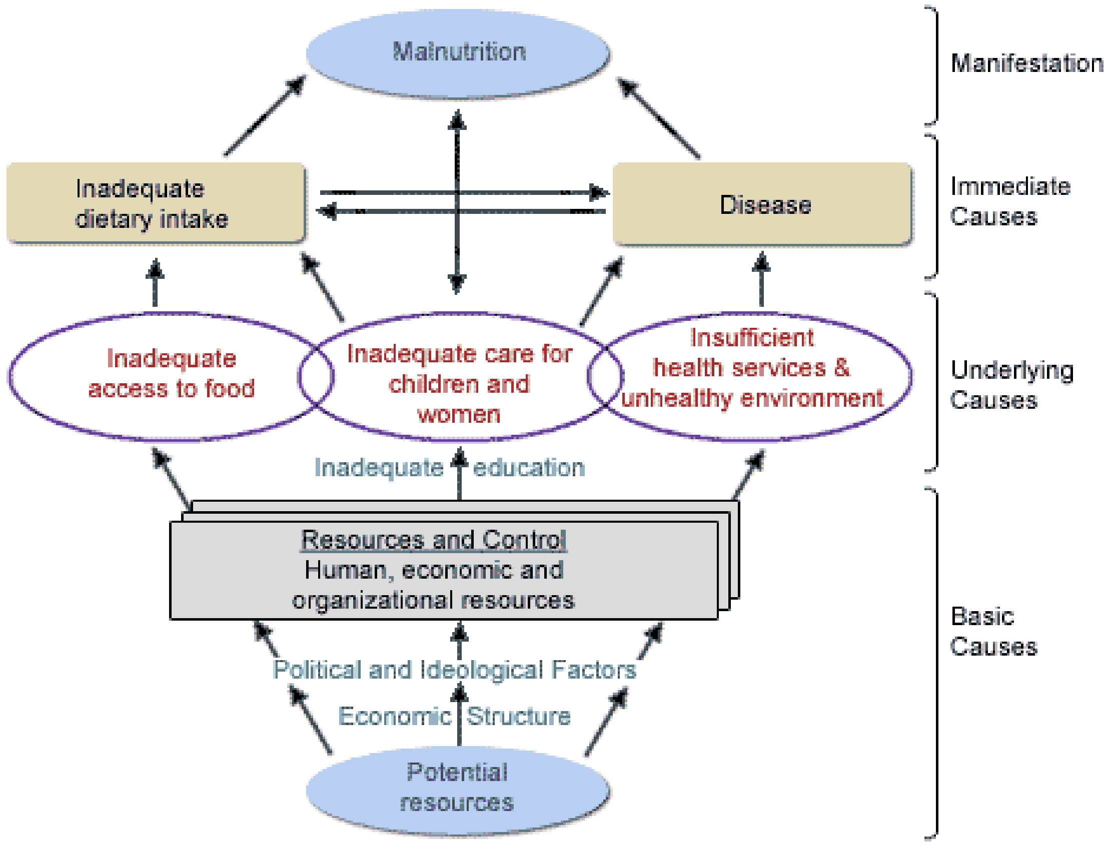

Figure 2.6Immediate, underlying, and basic causes of malnutrition (UNICEF2004).

The framework categorizes the causes of malnutrition as basic, referring to poor economic and political structures; immediate, referring to poor dietary intake, psycho-social stress and trauma and diseases such as diarrheal and acute respiratory conditions, which further complicate malnutrition; and underlying causes, referring to household food insecurity, lack of knowledge and education, caring practices and health services, as well as an unhealthy environment. Hunger and under-nutrition arise from poor food consumption, poor care, and unhealthy facilities, and, indirectly, through agricultural barriers, lack of employment opportunities and women's status in society [Klugman, 2014; Kurz & Johnson, 2001; World Health Organization, 2001].

On a different outlook Srivastava *et al.,* (2012) mentioned "geographical relocation from rural areas to urban localities exposes migrants to new environmental challenges. Urban slum dwellers are exposed to poor environmental conditions (overcrowding, poor quality drinking water, poor sanitation, and poor waste disposable facilities). Ignorance and difficult conditions of life in the slums are likely to result in improper food habits, low health care use and hygiene awareness and lack of knowledge of the origin of sickness and proper measures for the cure. The situation is further worsened due to lack of necessary health centers, medicines, and health care personnel. Children living under such conditions are at especially high risk for health and nutritional problem".

In Kenya, a study investigated the direct and indirect effects of economic poverty on child outcomes, the results suggested that in infancy, impaired psychomotor development is associated directly with undernutrition, while the effect of poverty is mediated entirely through nutritional status [Abubakar *et al.*, 2008].

As A.K. Shiva Kumar (2012) writes, "The denial of as little as 200-300 calories in a young child's daily diet is what makes the difference between the normal growth and the faltering that starts the descent towards illness and death."

Undernutrition continues to be high and progress toward reaching Millennium Development Goal 1 has been slow. Previously unrecognized extremely poor breastfeeding and complementary feeding practices and lack of comprehensive data on intervention coverage require urgent action to improve child nutrition [Lutter *et al.,* 2011]. Overall, 52.5% of all deaths in young children were attributable to undernutrition, varying from 44.8% for deaths because of measles to 60.7% for deaths because of diarrhea [Caulfield *et al.*, 2004].

Joshi *et al.,* (2011) revealed highly significant association ($p<0.005$) of maternal factors like literacy, occupation, diet knowledge and monthly per-capita income respectively with child nutrition.

2.7 *The vicious cycle of Undernutrition and Infection*

"Infectious disease is the major cause of morbidity and mortality in developing countries, particularly in children. Increasing evidence suggests that protein-calorie malnutrition is the underlying reason for the increased susceptibility to infections observed in these areas. Moreover, certain infectious diseases also cause Undernutrition, which can result in a vicious cycle" [Rodriguez *et al.,* 2011].

Borelli *et al.,* (2004) said "The malnutrition-infection complex can be viewed under two aspects, malnutrition compromising host defense, or infection either aggravating a previously existing deficient nutritional status or triggering malnutrition through disease pathogenesis. Malnutrition can facilitate pathogen invasion and propagation; further, it can increase the probability of a secondary infection occurring, thus modifying both disease pathogenesis and prognosis".

Schaible and Kaufmann, (2007) in their article "Malnutrition and infection: Complex mechanisms and global impacts discussed "the apparent vicious cycle involved, where malnutrition increases disease susceptibility and disease causes a reduction in food intake. They further quoted "the relationships among malnutrition, immune suppression, and infection are complicated by the severe effects that a number of infections exert on nutrition. Examples of how infections can contribute to malnutrition include: (1) gastrointestinal infection that lead to diarrhea, (2) chronic infections that cause cachexia and anemia; and (3) intestinal parasites that cause anemia and nutrient deprivation".

Needless to say that infection can suppress appetite and directly affect nutrient metabolism, leading to poor nutrient utilization. Bhargava *et al.* (2014) also said that undernutrition is the commonest cause of immunodeficiency worldwide, affecting innate as well as adaptive immune responses. Fig. 2.7 depicts some of the key interactions that are responsible for altered immune response in undernourished host during infection exposure.

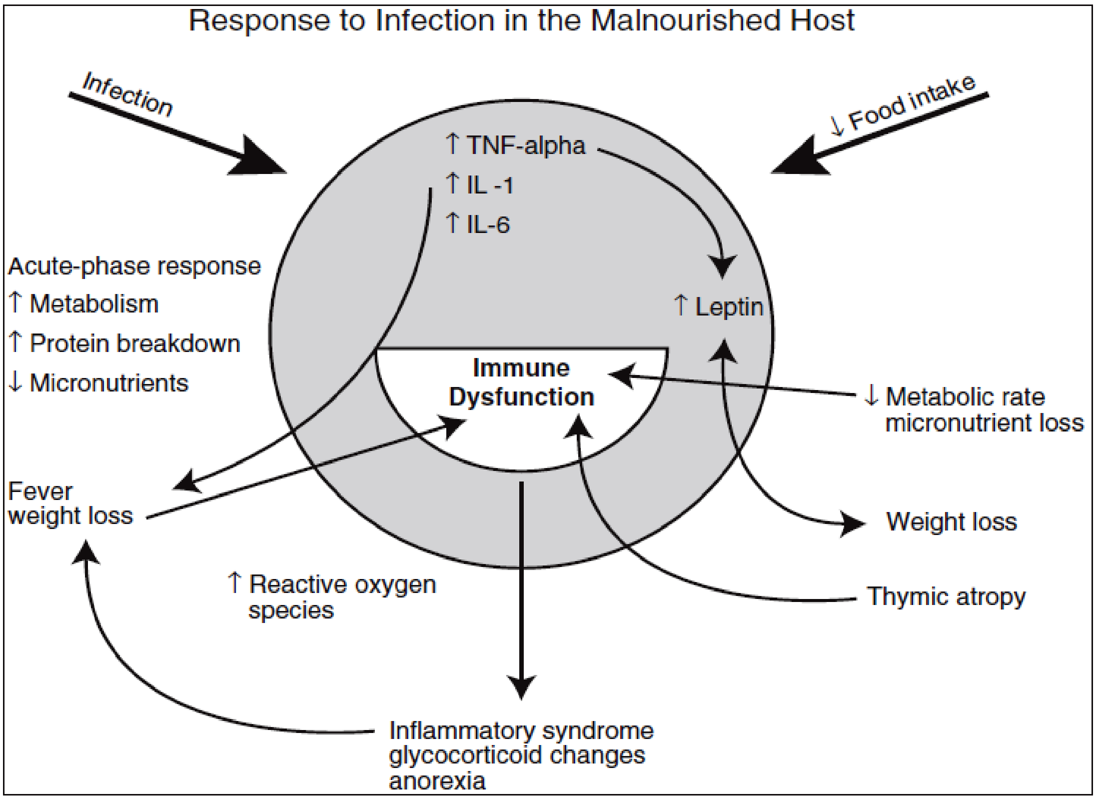

Fig.2.7Immune response in malnourished host during infectious.
IL = intereleukin; TNF = tumor necrosis factor.
[Source: Rundles *et al.*, 2008].

Among the principal causes of death in young children, 60.7% of deaths as a result of diarrhea, 52.3% of deaths as a result of pneumonia, 44.8% of deaths as a result of measles, and 57.3% of deaths as a result of malaria are attributable to undernutrition [Caulfield *et al.,* 2004]. Singh *et al.*(2014)

reported the most common morbidities in the undernourished school children of Bareilly district of Uttar Pradesh were upper respiratory tract infection 240 (42.78%), diarrhea 81 (14.44%). In a cross-sectional survey conducted in Assam, by Talukdar and Baruah (2015), it was found, that out of 400 school children majority 34.75% of school children were suffering from fever in the last 4 weeks followed by ARI/Acute respiratory infection (31.75%).

The relationship between diarrhea, particularly persistent diarrhea, and malnutrition is bidirectional and it is not possible to determine the extent to which malnutrition may be due to persistent diarrhea [Amadi *et al*., 2005; Nel, 2010].

2.8 *Role of Immunity and Immunoglobulin A (IgA) in nutrition and infection*

In biology, immunity is the balanced state of having adequate biological defenses to fight infection, disease, or other unwanted biological invasion, while having adequate tolerance to avoid inflammation, allergy, and autoimmune diseases (Wikipedia, 2015). And human biological system has a complete unit called "Immune system" (Fig. 2.8) devoted to keep us immune. The organs of the immune system are positioned throughout the body. They are called lymphoid organs because they are home to lymphocytes, small white blood cells that are the key players in the immune system [USDHHS, 2003]. Immunity depends on an intricate homeostatic system aimed at maintaining a delicate balance between health and disease. Its function is maintained by a series of complex, highly regulated, multi-cellular, physiologic mechanisms designed to accomplish a singular goal: to differentiate self from non-self. The healthy immune system has the ability to distinguish between the body's own cells, recognized as "self" and foreign cells, or "non-self" [WHO, 2009].

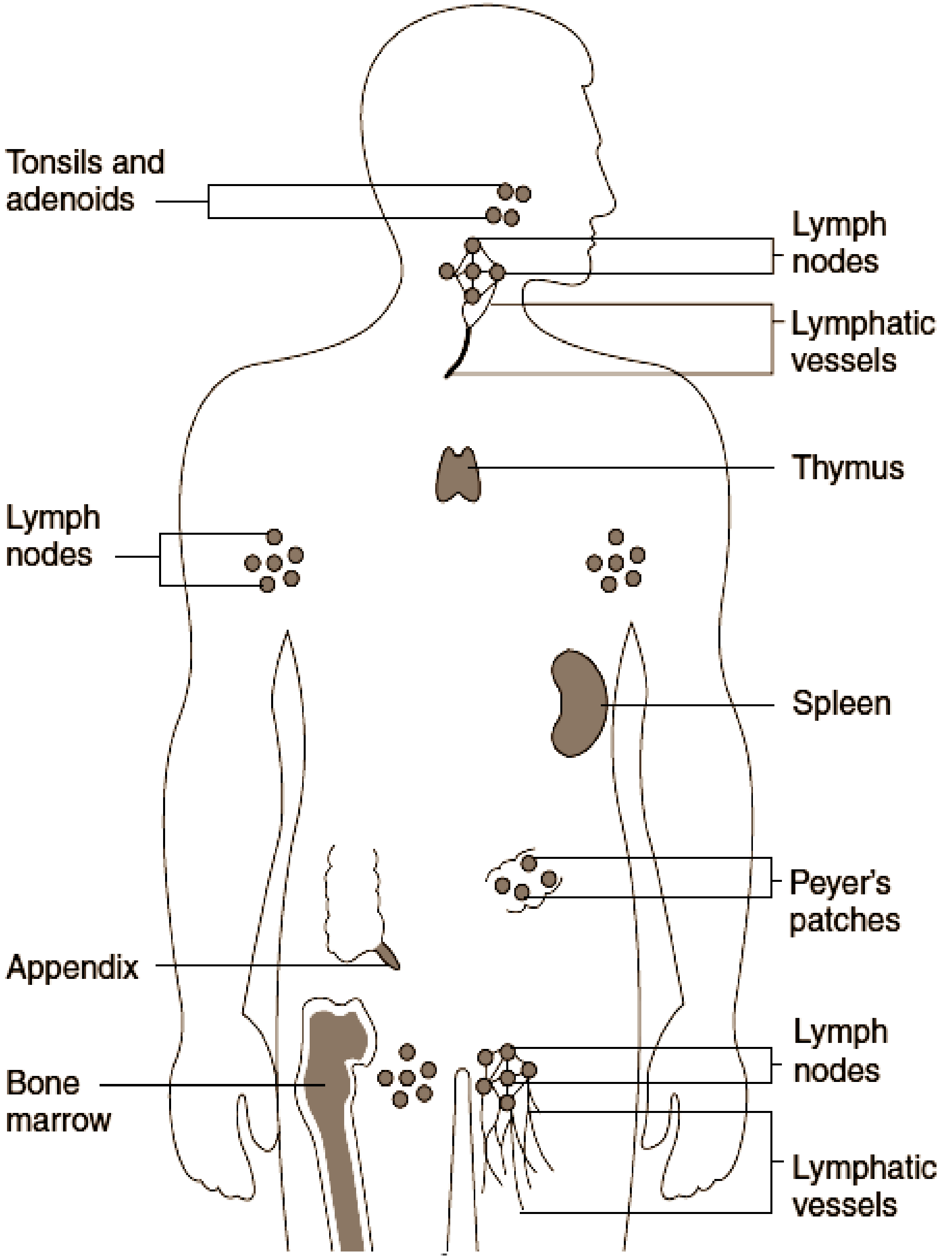

Fig. 3.8Various organs involved in Immune System

The immune system stores just a few of each kind of the different cells needed to recognize millions of possible enemies. When an antigen appears, those few matching cells multiply into a full-scale army. After their job is done, they fade away, leaving sentries behind to watch for future attacks [USDHHS, 2003].

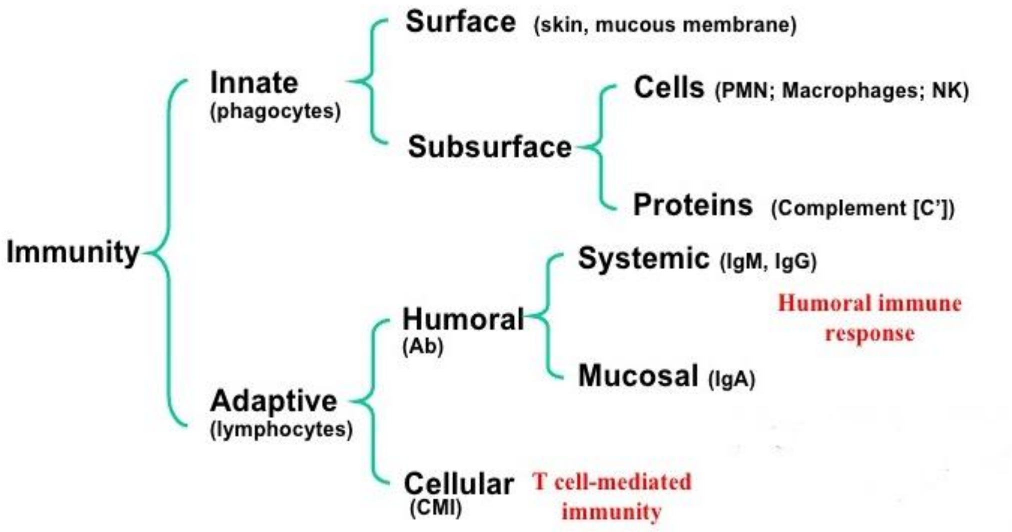

Fig. 2.9 Concept Map of Immunity

(Source: Eric Sobel, www.imgbuddy.com)

Eric Sober clearly explains the classification of immune system as given in fig 2.9.The two main types of lymphocytes are known as T and B cells. These two types of lymphoid cells are developed and differentiated in the primary lymphoid organs.

As mention by Dr. Sridhar Rao [www.microrao.com] "the production of new lymphocytes, or lymphopoiesis, takes place in specialized lymphoid tissues—the central lymphoid tissues—which are the bone marrow for most **B cells** and the thymus for most **T cells**. Lymphocyte precursors originate in the bone marrow, but whereas B cells complete most of their development there, the precursors of most T cells migrate to the thymus, where they develop into mature T cells.

The principal functions of B cells are to make antibodies in response to antigens, to perform the role of antigen-presenting cells, and to develop into memory B cells after activation by antigen interaction [Mauri and Bosma, 2012].

An antibody, also known as an immunoglobulin (Ig), is a large, Y-shape protein produced by plasma cells that is used by the immune system to identify and neutralize pathogens such as bacteria and viruses. The antibody recognizes a unique molecule of the harmful agent, called an antigen, via the variable region [Charles, 2001; Litman *et al*., 1993]. Circulating antibodies comprise of five classes; IgG, IgA, IgM, IgD and IgE. IgM and IgG dominate systemic immunity [Bode, 2012].

Immunoglobulin A (IgA) is the first line of defense in the resistance against infection, via inhibiting bacterial and viral adhesion to epithelial cells and by neutralization of bacterial toxins and virus, both extra- and intracellularly [Rhonda, 2014]. It is the predominant antibody in the secretions that bathe mucosal surfaces such as the gastrointestinal, respiratory, and genito-urinary tracts and in external secretion such as colostrums, milk, tears and saliva. It is the second most prevalent immunoglobulin after IgG. Although IgG is present at around 5 time greater concentration than IgA, it is metabolized about 5 times more slowly, suggesting both IgA and IgG are similar [Kaetzel, 2007]. It eliminates pathogens or antigens via an IgA-mediated excretory pathway where binding to IgA is followed by polyimmunoglobulin receptor-mediated transport of immune complexes.

This complex system of immunity is more complexed in terms of undernourished host. As mentioned by Prendergast (2015) that the immunology of malnutrition remains poorly characterized, but is associated with impairments in mucosal barrier integrity, and innate and adaptive immune dysfunction.

During the years 1998-99 it has been reported that total IgA concentration is reduced in the intestinal mucosa of protein-malnourished mice [McMurray, 1998 and Nikawa *et al*., 1999].

Rodriguez *et al*., [2011] suggests "that protein malnutrition may decrease IgA content by suppressing the proliferation and/or maturation of IgA-producing B-cells. Protein malnutrition suppresses the expression of the epithelial IgA-transporting protein, which decreases the total IgA concentration in the intestinal lumen. Thus, malnutrition appears to impair IgA-dependent mucosal immune defenses, including the production of IgA by plasma cells and its secretion into the lumen of the intestine".

Scarcity of published literature for serum IgA in terms of undernourished Indian school going children persuaded the investigators of present work to explore this parameter.

2.9 *Prevention strategies for Undernutrition*

"The current momentum within developing countries and internationally to address the problem of child undernutrition has never been higher" [Lancet, 2013]. Smith and Haddad (2015) revealed that "the rise of the **Scaling Up Nutrition (SUN) movement**, starting in 2010, and the publication of the Lancet Maternal and Child Nutrition Series in 2008 have both served to raise awareness of the extent and consequences of child undernutrition". A further marker of this commitment is the inclusion of "Food Security and Good Nutrition" (including indicators on child stunting and wasting) as one of 12 Development Goals proposed in the UN's High Level Panel on Development After 2015".

Gillespie *et al.* (2013) believed that Nutrition has consequently been greatly elevated on the global development agenda, and the global commitment to reducing undernutrition is stronger than ever.

Similarly Madan *et al.* (2014) suggested that "there is a felt need to enhance the quality of eating of children from high and low socio economic strata by imparting nutrition education and working out practical action plans based on locally available food resources to make the implementation cost effective. This is an important need of the hour and a challenge for nutritionist across the country. In addition multiple stake holders including school management, teachers, parents, media, NGOs, social networking groups and celebrities have to join hands to encourage healthy lifestyle practices and be a role model for our younger generation".

With respect to the basic causes of child undernutrition, the emphasis has been on building an enabling environment for undernutrition reduction through rigorous impact evaluations of nutrition programs, advocacy strategies, investment in building capacity, domestic resource mobilization, and politics and governance [Lancet, 2013]. There is a growing focus on understanding how factors such as political commitment, leadership, and accountability can create a more supportive environment for child nutrition" Beyond factors with a nutrition focus, the evidence on the key importance of income growth continues to accumulate [Headey *et al*., 2015; Ruel, 2013].

School feeding program is another successful approach for battling undernutrition. As UNICEF (2006) also mentioned that "in many parts of the world, children arrive at school with empty bellies. They may miss their morning meal, not get enough or the right things to eat, or be required to participate in family labour before school. As a result, they come to school with little energy to concentrate, engage with their teachers and classmates, or participate in physical education and other practical learning situations. These hungry children are more prone to low performance, to be absent from school, to fall sick and to drop out." An estimated 115 million school-aged children around the globe are out of primary school due to the lack of proper nutrition [UNICEF, 2005].

School feeding programmes offer the opportunity to alleviate hunger – both overt and hidden – among children. But their benefits go beyond nutrition. Studies have found that school feeding programmes provide an incentive for parents to send their children for an education, encourage children to stay in school and help them to focus and retain what they learn [UNICEF, 2006]. World Food Programme which works in collaboration with UNICEF aims to provide an integrated package of cost-effective interventions to improve the nutritional status and health of schoolchildren. Food for Education, an essential component of this package, seeks to alleviate short-term hunger in schoolchildren, increase parents' motivation and enhance community participation in schools" [World Food Programme, 2005].

UN Girls' Education Initiative [UNGEI, 2005] technical meeting recommended "school feeding programmes as part of an essential learning package to accelerate quality education for all. The recommended package also includes intervention areas such as water and sanitation, deworming and micronutrient supplementation".

In India, the school feeding program is known as ''Mid Day Meal Scheme (MDM)"to fight issues like hunger and malnutrition. Akshaya Patra Foundation, a not-for-profit organisation headquartered in Bengaluru, India presently implementing the Mid-Day Meal Scheme in the Government schools and Government aided schools. It is the world's largest (not-for-profit run) mid-day meal programme serving wholesome food to over 1.4 million children from 10,845 schools across 10 states in India [www.akshaypatra.org].

Nambiar and Desai (2012) from their research concluded that use of a Positive Deviance Approach and Behavior Change Communication strategy with the Mid Day Meal (MDM) staff, teaching staff as well as the students helped to bring about a change in various positive practices related to quality of MDM namely cleanliness, food handling storage and serving and monitoring by teachers.

Even in Bangladesh as reported by Ahmed (2004) aprrox. 1 million children received a mid-morning snack of biscuits that provided energy and sufficient amount of the daily requirement of vitamins and minerals. After a year, the programme raised net primary school enrolment by almost 10 per cent, and reduced the probability of dropping out by 7.5 per cent.

2.10 *The Intestinal Microbiota*

Hippocrates has been quoted as saying "death sits in the bowels" and "bad digestion is the root of all evil" in 400 B.C. showing that the importance of the intestines in human health has been long recognized.

Virtually all multicellular organisms live in close association with surrounding microbes, and humans are no exception. The human body is inhabited by a vast number of bacteria, archaea, viruses, and unicellular eukaryotes. The collection of microorganisms that live in peaceful coexistence with their hosts has been referred to as the microbiota, microflora, or normal flora [Sekirov *et al.*, 2010].

"During the co-evolution of man and microbes, the human intestinal tract is colonized by some thousand species of bacteria. Gut borne microbes out number the total of body tissue cells by a factor of ten. Recent metagenomics analysis of the human gut microbiota has revealed the presence of some **3.3 million genes**, as compared to the **mere 23thousand** genes present in the cells of the human body tissues" [Gutmicrobiota, 2012].

Papoff *et al.* (2012) revealed that "obligate anaerobes present in the gut include *Bifidobacterium, Clostridium, Eubacterium, Fusobacterium, Peptococcus, Peptostreptococcus,* and *Bacteroides,* and *facultative anaerobes Lactobacillus, Bacillus, Streptococcus, Staphylococcus, E. coli, Klebsiella,* and *P. aeruginosa*". As reported by Guarner and Malagelada (2003), 80% of cultivable bacteria in infants and 25% of it adults are *Bifidobacterium.* Fig 2.10 depicts the typical composition of human gut flora.

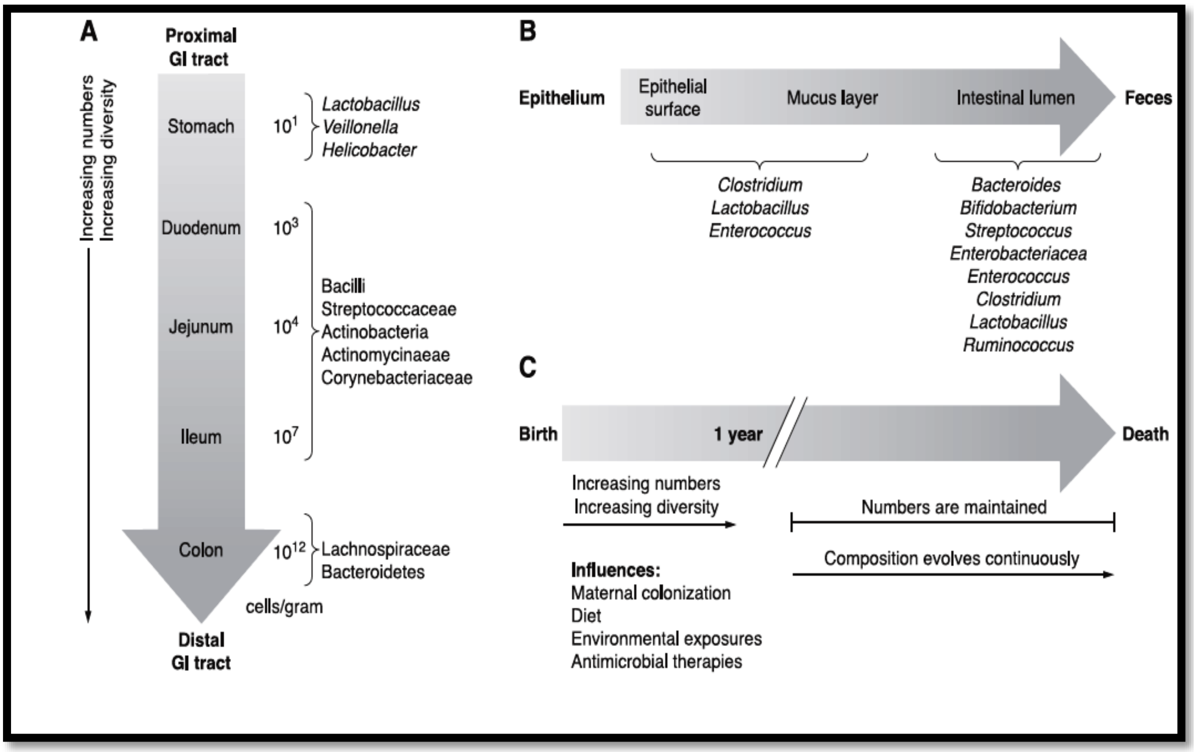

Fig. 2.10Spatial and temporal aspects of intestinal microbiota composition. A: variations in microbial numbers and composition across the length of the gastrointestinal tract. B: longitudinal variations in microbial composition in the intestine. C: temporal aspects of microbiota establishment and maintenance and factors influencing microbial composition. Source: Sekirov *et al.* (2010).

According to O'Hara and Shanahan (2006) "the intestinal microbiota is not homogeneous. The number of bacterial cells present in the mammalian gut shows a continuum that goes from 10^1 to 10^3 bacteria per gram of contents in the stomach and duodenum, progressing to 10^4 to 10^7 bacteria per gram in the jejunum and ileum and culminating in 10^{11} to 10^{12} cells per gram in the colon". The gastrointestinal tract is subjected to enormous and continual foreign antigenic stimuli from food and microbes. This organ must integrate complex interactions among diet, external pathogens, and local immunological and non-immunological processes. It is critical that protective immune responses are made to potential pathogens, while hypersensitivity reactions to dietary antigens are minimized [Schley and Field, 2002].

2.11 *Metabolomics of colonic microbiota in the gut*

The human gut is populated by an array of bacterial species, which develop important metabolic and immune functions, with a marked effect on the nutritional and health status of the host [Laparra and Sanz, 2010].

The gastrointestinal associated lymphoid tissues (GALT) comprise a secondary lymphoid tissue where effector immune responses directed gastrointestinal pathogens occur. Peyer's patches, an example of GALT, are aggregates of lymphoid follicles located along the small intestinal mucosa that protects the body; they respond to antigens that have passed through mucosal surface barriers [Rodriguez*et al.*, 2011].

Structurally, Peyer's patches contain proliferating B-lymphocytes, dendritic cells, macrophages and T-cells. Antigens in the lumen of the gut are transported to the Peyer's patches and initiate the immunologic response. This response is principally mediated by IgA production from activated B lymphocytes. This secretory IgA is released into the intestinal lumen. The main function of secretory IgA is to neutralize foreign pathogens by preventing binding to and penetration of epithelial cells. Moreover, the secreted cytokines for the epithelial barrier, part of mucosal immunity, regulate local immune responses [Erickson and Hubbard, 2009].

Sekirov *et al.* (2010) mentioned in their review that "the importance of the gut microbiota in the development of both the intestinal mucosal and systemic immune systems can be readily appreciated from studies of Germ Free (GF=microbiota lacking) animals. GF animals contain abnormal numbers of several immune cell types and immune cell products, as well as have deficits in local and systemic lymphoid structures. Spleens and lymph nodes of GF mice are poorly formed. GF mice also have hypoplastic Peyer's patches and a decreased number of mature isolated lymphoid follicles. The number of their IgA-producing plasma cells is reduced, as are the levels of secreted immunoglobulins (both IgA and IgG). They also exhibit irregularities in cytokine levels and profiles and are impaired in the generation of oral tolerance".

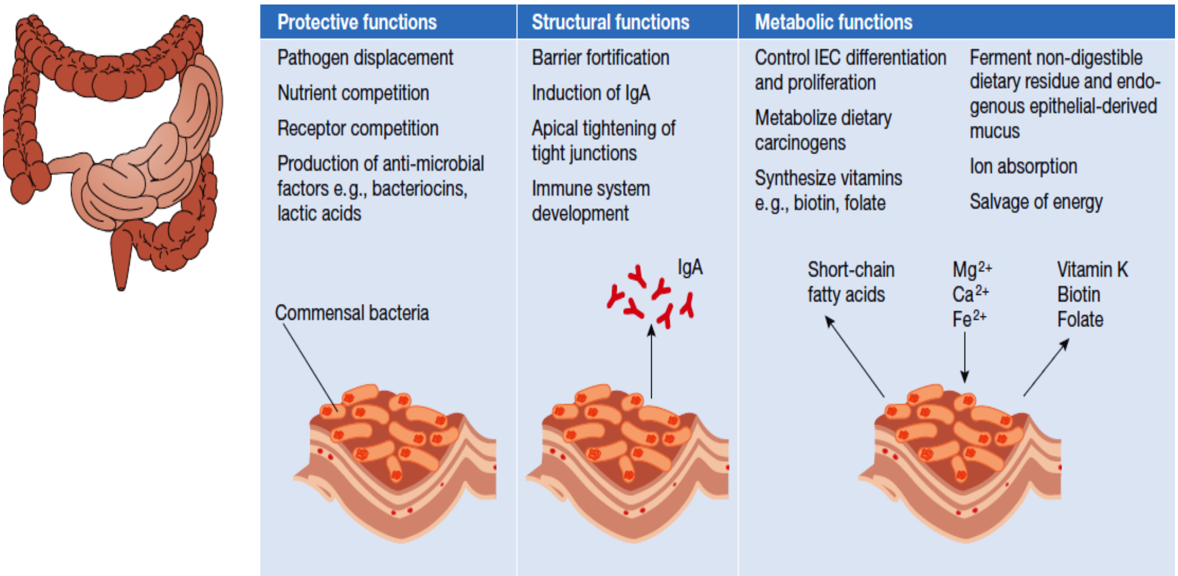

Fig. 2.11Commensal bacteria exert a miscellany of protective, structural and metabolic effects on the intestinal mucosa.
[Source: *O'Hara and Shanaha, 2006*]

O'Hara and Shanaha (2006) explain the various functions carried out by the gut flora (Fig.2.11). Human gut is not only capable of removing pathogens but also induction of various defense mechanisms in order to protect the over-all physiology like production of IgA and SCFA (Short Chain Fatty Acid).

2.12 *Gastrointestinal health and its significance in immunity and Undernutrition*

Since the discovery of *Bifidobacteria* by Tissier in 1900 century much attention has been directed to the habitat, nutritional and immunological role, biochemistry, and taxonomy of these bacteria. Gut microbiota provides its host with a physical barrier to incoming pathogens by competitive exclusion, such as occupation of attachment sites, consumption of nutrient sources, and production of antimicrobial substances. It also stimulates the host to produce various antimicrobial compounds [Sekirov *et al.*, 2010].

Various studies [Qin *et al.*, 2010; Ashida *et al.*, 2012; DuPont and DuPont, 2011] revealed abnormal and impaired microbiota in many diverse diseases such as inflammatory bowel diseases, colorectal cancer, irritable bowel syndrome, metabolic syndrome, or non-alcoholic fatty liver disease. Backing the fact that gut microflora is one of the essential organ for the perfect "Homeostasis" of our body.

Schley and Field (2002) explains "A mucosal immune system (containing defenses of both the innate and the acquired immune systems) is strategically placed in areas where external pathogens and antigens may gain access to the body. This includes the mucosal associated lymphoid tissues, which protect sites such as the respiratory, urinary and reproductive tracts, and **GALT (Gut Associated Lymphoid Tissue), which protects the intestine**. As the intestine is the first line of defense from the environment, and must integrate complex interactions **among diet, external pathogens, and local immunological and non-immunological processes**, it is critical that protective immune responses are made to potential pathogens, yet it is equally important that hypersensitivity reactions to dietary antigens are minimized".

2.13 *Factors affecting intestinal microbiota and health*

Mandar and Mikelsaar (1996) reported the evidence that the immediate contact with microbes during birth can affect the development of the intestinal microbiota, comes from the fact that the intestinal microbiota of infants and the vaginal microbiota of their mothers show similarities. Additionally, infants delivered through cesarean section have different microbial compositions compared with vaginally delivered infants (Huurre *et al.*, 2008).

Studies [Ecberg *et al.*, 2005; Gill *et al.*, 2006] revealed composition in the human gut. It is perhaps surprising that the composition of the human microbiota is fairly stable at the phylum level. The major groups that dominate the human intestine are conserved between all individuals, although the proportions of these groups can vary. However, when genera and species composition within the human gut is analyzed, differences occur. Within phyla, the inter individual variation of species composition is considerably high.

Vrieze*et al*. (2010) stated that "at the age of 4 years, the gut microbiota in host individuals has fully matured. The final composition of the microbiota is influenced by the host genotype, colonisation history, the physiology of the host and an array of environmental factors Genetic makeup of the individual also influences the composition of the core microiota."

Laparra and Sanz (2010) found various dietary factors impacting gut microflora, they stated "Dietary component also play beneficial roles beyond basic nutrition, leading to the development of the functional food concept and nutraceuticals”. Polyunsaturated fatty acids (PUFAs) and Phytochemicals are the most well characterized dietary bioactive compounds”. **PUFAs** include the ω-3 and ω-6 fatty acids, whose balance may influence diverse aspects of immunity and metabolism. **Phytochemicals** and their metabolic products may also inhibit pathogenic bacteria while stimulate the growth of beneficial bacteria, exerting prebiotic-like effects. Therefore, the intestinal microbiota is both a target for nutritional intervention and a factor influencing the biological activity of other food compounds acquired orally (Fig. 2.12).

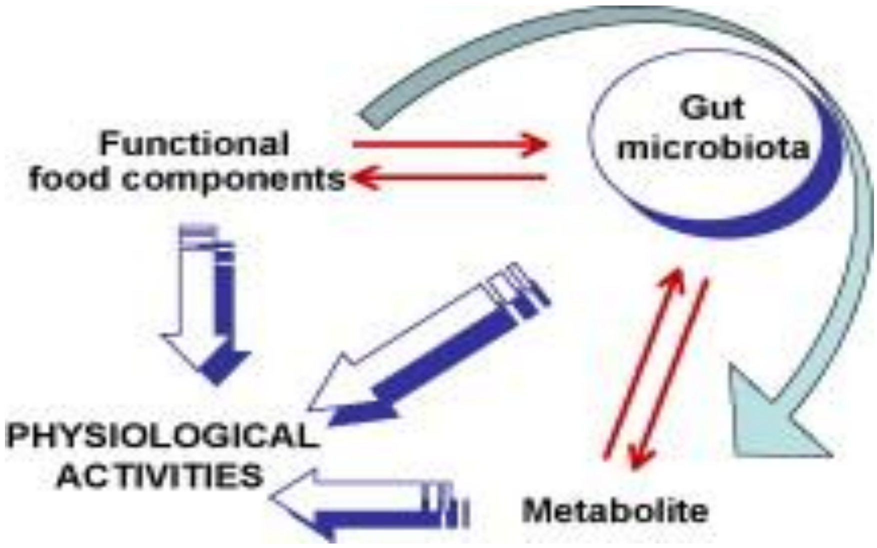

Fig. 2.12Factors impacting gut microbiota [Source: Laparran and Sanz, 2010]

Moschen *et al.* (2012) in their review titled “Dietary Factors: Major Regulators of the Gut’s Microbiota” demonstrated that there might exist a huge impact of environmental factors such as diet on the gut’s microbiome. They have also listed the impact of a particular diet on various microbes residing in gut (Fig.2.13).

Dietary intervention	Change in microbiota
High-fat diet	Bacteroidetes ↓
	Firmicutes ↑
	Proteobacteria ↑
High-fat/High-sugar diet	Bacteroidetes ↓
	Firmicutes ↑ (Erysipelotrichi, Bacilli)
Protein-rich/Saturated fats	"*Bacteroides*" enterotype
Carbohydrate-enriched diet	"*Prevotella*" enterotype
Self-reported vegetarians	"*Prevotella*" enterotype
High fiber content	Bacteroidetes ↑ , Actinobacteria ↑
	Firmicutes ↓ , Proteobacteria ↓
Western diet	"*Bacteroides*" enterotype
Vegetarian lifestyle	*Bacteroides* spp. ↓ , *Enterobacteriaceae* spp. ↓
	Bifidobacterium spp. ↓ , *Escherichia coli* ↓

Fig. 2.13Effect of Various Diets on the Intestinal Microbiota

Therefore it can be assume that one's gut is not only dependent one one's genetic make-up but the way one is delivered from the womb, his breast feeding practices, kind of diet one follows and other numerous factors.

2.14 Role of Prebiotics in enhancing good Gutmicroflora viz. Bifidobacteria and Lactic acid bacteria

Microbiomics has spurred a dramatic increase in scientific, industrial and public interest in probiotics and prebiotics as possible agents for gut microbiota management and control. Genomics and bioinformatics tools may allow us to establish mechanistic relationships between gut microbiota, health status and the effects of drugs in the individual, hopefully providing perspectives for personalized gut microbiota management (Gutmicrobiota, 2012).

The term "prebiotic" was first coined and introduced in 1995 by Glenn Gibson and Marcel Roberfroid, who exchanged "pro" to "pre" which means "before". [Aida *et al*., 2009]. The definition was updated in 2004 when prebiotics were defined as **"selectively fermented ingredients that allow specific changes, both in the gastrointestinal microflora that confer benefits upon host well-being and health."** The definition considers microflora changes in the whole gastrointestinal tract and as such extrapolates the definition into other areas that may benefit from a selective targeting of *Bifidobacteria* and *Lactobacilli* [Bellei and Haslberger, 2013].

The criteria used for classification of a food ingredient as a prebiotic are as follows:

- Resistance to digestive processes in the upper gastrointestinal tract.
- Fermentation by gastrointestinal microbiota.
- Selective stimulation of growth and/or activity of beneficial bacteria which are associated with health and well-being.

There is increasing evidence that fermentable dietary fibres and the newly described prebiotics can modulate various properties of the immune system, including those of the gut-associated lymphoid tissues (GALT) [Schley and Field, 2002].

Seifert and Watzl (2007) revealed that prebiotics like Oligofructose and Inulin immunological impacts Peyer's Patches as well as other tissues of the GALT via following stated mechanisms:

Potential mechanisms of prebiotic-induced immunomodulations

- Selective increase/decrease in specific intestinal bacteria that modulate local cytokine and antibody production
- Increase in intestinal SCFA production and enhanced binding of SCFA to G-coupled protein receptors on leukocytes
- Interaction with carbohydrate receptors on intestinal epithelial cells and immune cells
- Partial absorption of Inulin/Oligofructose resulting in local and systemic contact with the immune system"

Schley and Field, 2002 suggested that there is increasing evidence that the addition of fermentable fibre to the di*et* alters the function and structure of the gut, modifies the production of gut-derived hormones, and is associated with improved whole body glucose homeostasis even in the absence of disease. *Lactobacilli* and *Bifidobacteria* are the usual target genera for prebiotics; changes in *Bifidobacteria* are more likely to be seen compared to *Lactobacilli*.This may be due to the fact that more *Bifidobacteria* usually reside in the human colon than *lactobacilli*, and they exhibit a preference for oligosaccharides [Slavin, 2013].

2.15 *Evolution of Fructooligosaccharide (FOS) as a prebiotic*

FOS is a carbohydrate that is not hydrolyzed in the human intestinal tract and thus is reduced in caloric value compared to other digestible carbohydrates. It can be used in food products as bulking agents, in place of sugar, with a resultant reduction in the energy content of the food.

The size and complexity of the FOS molecule gives it desirable characteristics. Although the simple sugars fructose and glucose are quickly absorbed into the body by the intestines, FOS for the most part is indigestible and therefore acts as a non-digestible fiber in the diet. This is because the human does not have the enzymes to break down the FOS as it travels down the digestive tract [Medicinal Food News, 1997].

FOS are composed of linear chains of fructose units, linked by $\beta(2\rightarrow1)$bonds, and often terminated by a glucose unit. The number of fructose units ranges from 2 to 7 [Ten*et al.*, 2006].

Saulnier *et al.* (2007) elaborate "Fructooligosaccharide include a diverse family of fructose polymers which vary in length and can either be derivatives of simple fructose polymers or fructose moieties attached to a sucrose molecule. Most fructooligosaccharides marketed as ingredients for foods and nutritional supplements are either synthesized from sucrose using fructosyl transferases derived from *Aspergillus niger* (short chain fructooligosaccharides [scFOS]) or extracted from chicory roots (*Cichoricum intybus*) by a partial enzymatic hydrolysis of inulin (FOS). Their general structure can be represented by GFn or Fn, in which G and F are, respectively, a glucose or fructose unit and n is the number of fructosyl units".

Anderson *et al.* (1999) revealed that FOS are not hydrolyzed by human small intestinal glycosidases and reach the colon intact. In the colon, FOS may specifically stimulate growth of endogenous *Bifidobacteria* and *Lactobacilli* [Tuohy *et al.*, 2001; Holma *et al.,* 2002]. The protective microflora and their subsequent production of organic acids may increase host resistance against acid-sensitive pathogens [Ten *et al.*, 2006].

FOS increased infection induced growth impairment, diarrhea, gut inflammation and permeability of the large intestine [Ten *et al.*, 2006].

2.16 *Role of Fructooligosaccharide in enhancing good gut bacteria viz. Bifidobacteria and Lactic acid bacteria and reducing the enteric pathogens*

Schneeman [1999] explained the behavior of oligofructose in the gut and it's further impact. He mentioned that "the compounds and fluids in food are mixed with the secretions of the stomach, small intestine, pancreas, and gallbladder. Although dietary fibers, like oligofructose, are not digested by the enzymes in the small intestine, their presence in the intestine may affect the physical characteristics of the gut contents. The fermentability of oligofructose provides a route by which they can increase stool weight because they would increase **microbial mass** in the colon. In addition, the fermentation can lower the pH of colon contents, and the production of **SCFA (short chain fatty acid)** is likely to affect the health of the intestinal mucosa".

When the FOS reaches the large intestine and the colon, the bacteria that are found there start to break down the FOS. These bacteria have the enzymes needed to break down FOS. ***Bifidobacteria*** have been reported to use FOS. It is believed that foods that promote ***Bifidobacteria*** growth are good for the health [Farnworth, 1997].

In a study with elderly people living in a nursing home, 3 week of Oligo Fructose supplementation at a dose of twice 4 g/d increased fecal bacterial counts of *Bifidobacteria* [Guigoz *et al.*, 2002]. Gibson *et al.* through their trial revealed that15-g /day dietary addition of oligofructose or inulin led to *Bifidobacterium* becoming the numerically predominant genus in feces. Thus, small changes in diet can alter the balance of colonic bacteria towards a potentially healthier microflora.

Bouhnik *et al.* [2006] obtained significant correlation between the ingested dose of FOS (short chain) and faecal *Bifidobacteria* counts at day 15 ($r^2 = 0.307$, $P < 0.001$) they also found out that the total anaerobes increased at the dose of 10 g/d.

Way back in 1995 Gibson *et al*., also found that "in vitro Oligosaccharide selectively stimulate the growth of species of *Bifidobacterium,* a genus of bacteria considered beneficial to health. This study was designed to determine their effects on the large bowel microflora and colonic function in vivo".

The FOS and inulin addition to yoghurt caused an increase in the numbers of all bacteria in comparison to control yoghurt obtained without addition of prebiotics. The viable counts of *Str. thermophilus*, *Lb. acidophilus* and *Bifidobacterium sp*. when 1% of FOS was added to yoghurt were about 9 log cfu/g, 7.8 log cfu/g and 7.7 log cfu/g, respectively [Gustaw *et al*., 2011].

FOS also improve bioavailability of minerals such as calcium, magnesium and iron, increase activity of beneficial live active cultures like *Lactic acid bacteria* and *Bifidobacteria* and inhibition of harmful bacteria like enteric pathogens in the digestive tract [Gustaw*et al*., 2011]. FOS fermentation increased fecal wet weight, B*ifidobacteria, Lactobacilli*, and *Lactic acid.*

Number of studies [Swanson *et al*., 2002; Fukushima *et al*., 1999; Qiao *et al*., 2002] suggests that ingestion of Bifidobacteria is associated with increased

IgA levels in the small intestine and feces and ex-vivo IgA production by Peyer's Patches B-lymphocytes.

The normal human intestinal flora that exerts several beneficial effects on human health and well-being. They produce short-chain fatty acids and improve the intestinal microbial balance, resulting in the inhibition of bacterial pathogens, reduction of colon cancer risk, and improving the immune system [Saarela *et al*., 2002; Tamime and Robinson, 2007].

2.17 *Role of FOS in improving Immunity and reducing Morbidity especially Diarrhea, Common cold constipation; Flatulence and Gut health*

Watzl *et al.* (2005) stated that “non-digestible carbohydrates may have an impact on the immune system, especially in the area of the gut-associated lymphoid tissue (GALT). Recent data now provide first evidence that prebiotics such as inulin/oligofructose (IN/OF) modulate functions of the immune system. In animal studies IN/OF primarily activated immune cells in Peyer's patches including IL-10 production and natural killer (NK) cell cytotoxicity. Other immune functions modulated by IN/OF included the concentration of secretory IgA in ileum and caecum, splenic NK cell cytotoxicity as well as splenocyte cytokine production. In different tumour models, a lower incidence of tumours was observed, which in the case of colonic tumours was associated with enhanced NK cell cytotoxicity in the GALT”.

Way back in 1998 Oli and his colleagues revealed that “secretary diarrhea disturbs the normal densities and relative species abundance of the microbiota, with the influences more pronounced for contents relative to the mucosa, and that adding FOS to OES accelerates the recovery of bacteria perceived as beneficial while potentially slowing the recovery of pathogenic forms”.

In a different relatable trial Ghanei *et al.* (2015) observed the scores of Atopic dermatitis (SCORAD) through the intervention of inulin+ fructooligosaccharide. Intervention resulted in a significant improvement in the total SCORAD score in treatment group compared to control group ($P<0.001$) and in significant decrease in serum IgE levels in the treated compared to control group ($P<0.001$), they concluded that prebiotic supplementation may have beneficial effects on serum IgE which may improve SCORAD.

Data from studies with infants suggest that supplementation with a prebiotic mixture positively affects postnatal immune development and increases fecal secretory IgA. Prebiotic Inulin/FOS (oligofructose) clearly modulates immunological processes at the level of the gut-associated lymphoid tissue, which may be associated with significant health benefits in infants and patients with intestinal inflammatory diseases [Seifert and Watzl, 2007].

The ultimate impact of a Prebiotic is due to the **Probiotic** they raise after ingestion and therefore trials involving prebiotics can considerably be used as a platform to define benefits of Prebiotics.

He *et al.* (2005) conducted a trial wherein four hundred and two preschool children (217 males, 185 females), aged 3-5 years, whose height for age and/or weight for age were less than the reference level, were selected as subjects from 7 kindergartens in Beijing Fangshan District. The subjects were divided randomly into control group (CG, 201) and yogurt supplemented group (YG, 201). Each subject in YG was given one serving of yogurt (125 g) for 5 days a while nothing additional was provided to CG. Study concluded that Yogurt is beneficial to the improvement of calcium, zinc, and vitamin B2 intake, the decreasing of the incidence and duration of upper-respiratory infection and diarrhea, and the promotion of the health and the growth and development of preschool children.

Oligosaccharides have been shown to interfere with leukocyte recruitment to sites of inflammation and to inhibit cell–cell interactions of leukocytes and lymphocytes via selectins [Eiwegger *et al*., 2010].

Nauta and Garssen (2013) in their review entitled "Evidence-based benefits of specific mixtures of non-digestible oligosaccharides on the immune system" optimistically expressed that "the current body of data on the immune modulatory properties of specific mixtures of oligosaccharides holds great promise for the prevention and or treatment of immune related disorders. Both the development of diseases such as allergies and infections in early life as well as a therapeutic effect in different immune-mediated inflammatory diseases later in life, including cancer and HIV can be affected by adding specific oligosaccharides to the diet".

2.18 Role of FOS in improving the nutritional status of children

Effectual researches are arid in terms of FOS trial for their impact on nutritional status of children which is one of the potent reasons to pursue this study further. Though, an explanation can always be drawn via learning FOS's numerous roles in benefiting the overall human physiology.

Vendrig *et al.* (2014) supported FOS as an immunomodulator prebiotic, having the beneficial properties of human milk and colustrum and undoubtedly human milk is ever known for its effect on nutritional status.

Further, Sangwan *et al.* (2011) says Galacto-oligosaccharides (GOS) often proven to be beneficial for health in several ways for instance by enhancing defensive immune responses [Gopalakrishanan *et al.*, 2012; Vos *et al.*, 2007 and Schijf *et al.*, 2012] and lowering the incidence of infections [Arslanoglu *et al.*, 2007 and Chatchatee *et al.*, 2014] and these are undoubtedly the indicatives of improved nutritional status.

Sazawal *et al.* (2010) conducted a community based double-masked, controlled trial in a peri-urban area of New Delhi (India) using milk fortified with *Bifidobacterium lactis HN019* and Oligosaccharides which was supplemented to children of 1-3 years of age for the period of 1 year. At the end of the trial prebiotic-fortified milk increased weight gain by 0.13 kg/year (95% CI 0.03, 0.23; P¼0.02) and reduced the risk of being anemic and iron deficient by 45% (95% CI 11%, 66%; P<0.01).

Other community-based randomized controlled trials have provided evidence that consumption of probiotic-supplemented formula or lactobacilli-acidophilus–fortified yogurt resulted in significantly accelerated growth of undernourished as well as adequately nourished preschool children [Saran *et al.*, 2002 and Nopchinda *et al.*, 2002].

A systematic review on effects of probiotics on child growth by Onubi *et al.* (2015) can also indirectly explain various benefits of dietary intake of prebiotics (as prebiotics are the manufacturer of probiotics) in weight and length/height gain, potentially in children who are under-nourished living in developing countries. They noted that the children in the probiotic groups had growth curves that were significantly higher than or closer to the WHO reference value than the children in the control groups Improvement in height-for-age z-scores in children who took probiotics compared to those in the control group was also evident in various studies compiled in this review. They explained, "Change in height-for-age z-scores indicates catch-up growth in children therefore, **probiotics may help in promoting compensatory growth of children with stunted growth**".

These data suggest that oligosaccharides act systemically and can also modulate immune responses in a microbiota-independent manner; however, more research is needed to identify the underlying mechanisms by which oligosaccharides modulate the immune system (Nauta and Garseen, 2013).